REMARKS

Claims 1-14 were pending. Claim 1 has been amended. Claims 2, 13 and 14 have been canceled. No new matter has been added.

1. Amendments to the Specification

In response to the Examiner's request for correction of informalities (misspellings) found in the Specification, Applicant has submitted amendments to correct the identified misspellings as well as several additional misspellings discovered as follows:

"chemical" was misspelled as **"chemico"**

1) page 4, line 19

"fact" was misspelled as "**fat**"

1) page 5, line 14

"**instance**" was misspelled as "**insctance**"

1) page 17, line 27

"**acquired**" was misspelled as "**aquired**"

1) page 22, lines 10 and 31
2) page 23, line 9

"**agents**" was misspelled as "**gents**"

1) page 24, line 20

At the request of the Examiner, Applicant also deleted the erroneous letter "o" found at page 17, line 32.

Said amendments contain no new matter.

Applicant is also submitting both a "clean copy and marked-up copy of said amendment".

2. Claim Objections

At the request of the Examiner, Applicant amended Claim 1 to recite "said exogenous or endogenous….". Claim 2 was canceled, rendering the objection to it moot.

3. Rejections Under 35 USC §112, ¶ 1

Claims 1-14 were rejected under 35 U.S.C. 112, first paragraph because the Examiner found they did not reasonably provide enablement for the method for all possible endogenous and exogenous species.

Applicants respectfully traverse. One skilled in the art, particularly in light of the extensive guidance provided in the specification, would be able to practice the claimed invention without undue experimentation. Indeed, paragraphs 0108 to 1019 are directed to selecting the shift reagent, while paragraphs 0111 to 0114 explain the parameters in selecting the nucleus. In particular paragraphs 0115 and 0121 explain how to identify the most suitable combination of SA and nuclei for the quantitative determination of cell uptake. Furthermore, use of MAS-NMR to determine the cellular compartment in which the exogenous or endogenous substance distributes is discussed, for example at paragraphs 0123 - 0159. Finally, measuring the compartmental concentration of the exogenous or endogenous substance is discussed at paragraphs 0160 - 0167. Furthermore, Example 1 sets forth a system of equations which may be used by the skilled artisan to easily calculate the compartmental concentration of the exogenous or endogenous substance. Example 2 includes a specific example, in which these equations are used in the method of the invention to determine the cellular uptake of acetylsalicylic acid in red blood cells. Given this extensive teaching, the skilled artisan is able to make and use the claimed invention without undue experimentation. Thus, Applicants submit that the rejection for lack of enablement should be withdrawn.

Claim 14 was rejected under 35 U.S.C. 112, first paragraph for alleged failure to comply with the written description requirement. In view of the cancellation of claim 14, this rejection is moot.

4. Rejections Under 35 USC §112, ¶ 2 and 35 USC § 101

Claims 13 and 14 were rejected under 35 U.S.C. §112, second paragraph for alleged indefiniteness because the Examiner found they did not recite necessary steps. Claim 13 was further rejected under 35 U.S.C.§101. The cancellation of claims 13 and 14 renders these rejections moot.

6. Rejections Under 35 USC §102/103

Claims 1-7, and 10-12 were rejected under 35 U.S.C. 102(b) as anticipated by or under 35 U.S.C. 103 as obvious over Calabi et al (J. Mag. Reson., 2002, IDS) ("Calabi"). Applicants respectfully traverse. As the Examiner admits (Office Action at 7) Calabi is directed to a method of determining the cellular uptake of MRI contrast agents ("MRI-CA"). However, the instantly claimed method enables the determination of the cellular uptake of ant type of molecule, whether exogenous or endogenous to the organism. Calabi neither teaches nor suggests use of the disclosed method to determine uptake of anything other than MRI-CA. Indeed, as explained in the instant specification, the method of Calabi is premised on the virtually identical structure of the MRI-CA and the lanthanide shift agent used:

> The rationale for this method relies on the complete isostructurality between the Gd-contrast agents (CA), which intra- or extra-cellular concentration has to be determined, and the lanthanide complex acting as shift agents (LIS agent). In other words, as both CAand LIS agent are supposed to show a very similar behavior (because of their isostructurality), the actual determinations of where the LIS agent is, i.e. its exact intra- or extra-cellular concentration, are deemed to substantially correspond to where the CA would be and to the CA intra- or extracellular concentration, respectively.

Specification, ¶ 0061. Thus, Calabi neither teaches nor suggests that the disclosed method is useful for determining the uptake of anything other than MRI-CAs that are structurally identical to the lanthanide shift agent. Therefore, based on Calabi one skilled in the art would have no expectation that the method disclosed therein could be used successfully to determine the uptake of any molecule, whether or not structurally identical to the lanthanide shift agent used. Consequently Calabi neither anticipates nor renders the claims obvious and Applicants request withdrawal of this rejection.

CONCLUSION

In view of the preceding remarks, it is believed that claims 1 and 3-12 are in condition for allowance.

If there are any questions remaining as to patentability of the pending claims, Applicants would very much desire to have a telephonic interview. The Examiner is invited to contact Applicants' undersigned attorney at the number below.

No fee is believed to be due with the filing of this Amendment. However, if any fees are deemed necessary, the Director is hereby authorized to charge such fees to Deposit Account No. 50-2168.

Favorable action is respectfully requested.

Respectfully submitted,

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